Abiraterone Acetate Tablets

Type of Posting                      Notice of Intent to Revise  
Posting Date                        27–Sept–2019               
Official Date                       To Be Determined, Revision Bulletin  
Expert Committee                    Chemical Medicines Monographs 3

In accordance with section 7.04 (c) of the 2015–2020 Rules and Procedures of the Council of Experts and the Pending Monograph Guideline, this is to provide notice that the Chemical Medicines Monographs 3 Expert Committee intends to revise the Abiraterone Acetate Tablets monograph.

Based on the supporting data received from a manufacturer awaiting FDA approval, the Expert Committee proposes to add Dissolution Test 3 to the monograph. Labeling information has been incorporated to support the inclusion of Dissolution Test 3.

- Dissolution Test 3 was validated using the Phenomenex Luna C18 (2) brand of L1 column. The typical retention time for abiraterone acetate is about 4 min.

The proposed revision is contingent on FDA approval of a product that meets the proposed monograph specifications. The proposed revision will be published as a Revision Bulletin and an official date will be assigned to coincide as closely as possible with the FDA approval of the associated product.

See below for additional information about the proposed text.2

Should you have any questions, please contact Jane Li, Associate Scientific Liaison (301-230-6345 or Jane.li@usp.org).

1 The addition of Dissolution Test 2 to the Abiraterone Acetate Tablets monograph is currently being proposed under the Pending Monograph process.

2 This text is not the official version of a USP–NF monograph and may not reflect the full and accurate contents of the currently official monograph. Please refer to the current edition of the USP–NF for official text.

USP provides this text to indicate changes that we anticipate will be made official once the product subject to this proposed revision under the Pending Monograph Program receives FDA approval. Once FDA approval is granted for the associated revision request, a Revision Bulletin will be posted that will include the changes indicated herein, as well as any changes indicated in the product’s final approval, combined with the text of the monograph as effective on the date of approval. Any revisions made to a monograph under the Pending Monograph Program that are posted without prior publication for comment in the Pharmacopeial Forum must also meet the requirements outlined in the USP Guideline on Use of Accelerated Processes for Revisions to the USP–NF.
Abiraterone Acetate Tablets

**DEFINITION**
Abiraterone Acetate Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of abiraterone acetate (C_{26}H_{33}NO_{2}).

**IDENTIFICATION**
- **A.** The retention time of the major peak of the Sample solution corresponds to that of the Standard solution, as obtained in the Assay.
- **B.** The UV spectrum of the major peak of the Sample solution corresponds to that of the Standard solution, as obtained in the Assay.

**ASSAY**
- **PROCEDURE**
  Solution A: 10 mM of ammonium acetate in water
  Mobile phase: See Table 1.

<table>
<thead>
<tr>
<th>Table 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time (min)</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>40</td>
</tr>
<tr>
<td>47</td>
</tr>
<tr>
<td>58</td>
</tr>
<tr>
<td>60</td>
</tr>
<tr>
<td>70</td>
</tr>
</tbody>
</table>

[NOTE—Protect solutions from light.]

**System suitability solution:** 0.625 mg/mL of USP Abiraterone System Suitability Mixture RS in acetonitrile. [NOTE—See Table 2 for relative retention times of the main components of the mixture.]

**Table 2**

<table>
<thead>
<tr>
<th>Name</th>
<th>Relative Retention Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>7-Ketoabiraterone acetate</td>
<td>0.42</td>
</tr>
<tr>
<td>α-Epoxabiraterone acetate</td>
<td>0.62</td>
</tr>
<tr>
<td>β-Epoxabiraterone acetate</td>
<td>0.66</td>
</tr>
<tr>
<td>Abiraterone</td>
<td>0.69</td>
</tr>
<tr>
<td>3-Deoxy-3-acetyl abiraterone-3-ene</td>
<td>0.85</td>
</tr>
<tr>
<td>Abiraterone acetate</td>
<td>1.0</td>
</tr>
<tr>
<td>Abiraterone ethyl ether</td>
<td>1.18</td>
</tr>
<tr>
<td>Abiraterone isopropyl ether</td>
<td>1.26</td>
</tr>
<tr>
<td>Anhydro abiraterone</td>
<td>1.29</td>
</tr>
<tr>
<td>3-Deoxy 3-chloroabiraterone</td>
<td>1.31</td>
</tr>
<tr>
<td>O-Chlorobutylabiraterone</td>
<td>1.33</td>
</tr>
</tbody>
</table>

**Table 1**

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Solution A (%)</th>
<th>Acetonitrile (%)</th>
<th>Ethanol (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>50</td>
<td>20</td>
<td>30</td>
</tr>
<tr>
<td>40</td>
<td>15</td>
<td>55</td>
<td>30</td>
</tr>
<tr>
<td>47</td>
<td>0</td>
<td>20</td>
<td>80</td>
</tr>
<tr>
<td>58</td>
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<td>20</td>
<td>30</td>
</tr>
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<td>20</td>
<td>30</td>
</tr>
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</table>

[NOTE—Protect solutions from light.]

**System suitability solution:** 0.625 mg/mL of USP Abiraterone System Suitability Mixture RS in acetonitrile. [NOTE—See Table 2 for relative retention times of the main components of the mixture.]

**Table 2**

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**Standard solution:** 0.625 mg/mL of USP Abiraterone Acetate RS in acetonitrile

**Sample solution:** Nominally equivalent to 0.625 mg/mL of abiraterone acetate in acetonitrile, prepared from NLT 20 powdered Tablets as follows. Transfer the powder to a suitable volumetric flask. Add 50% of the flask volume of acetonitrile, shake by mechanical means for 30 min, and dilute with acetonitrile to volume. Pass a portion of the solution through a suitable filter of 0.45-μm pore size, and use the clear solution for analysis.

**Chromatographic system**
(See Chromatography (621), System Suitability.)

**Mode:** LC
**Detector:** UV 254 nm or diode array. [NOTE—Use a diode array detector to perform Identification B.]
**Column:** 3-mm × 15-cm; 3-μm packing L1
**Column temperature:** 15°
**Flow rate:** 0.45 mL/min
**Injection volume:** 10 μL

**System suitability**

**Samples:** System suitability solution and Standard solution

**Suitability requirements**

**Resolution:** NLT 1.0 between anhydro abiraterone and 3-deoxy 3-chloroabiraterone peaks, System suitability solution

**Relative standard deviation:** NMT 2.0%, Standard solution

**Analysis**

**Samples:** Standard solution and Sample solution

Calculate the percentage of the labeled amount of abiraterone acetate (C_{26}H_{33}NO_{2}) in the portion of Tablets taken:

\[
\text{Result} = \left( \frac{r_{U}}{r_{S}} \right) \times (C_{U}/C_{S}) \times 100
\]

- \( r_{U} \) = peak response from the Standard solution
- \( r_{S} \) = peak response from the Sample solution
- \( C_{U} \) = concentration of USP Abiraterone Acetate RS in the Standard solution (mg/mL)
- \( C_{S} \) = nominal concentration of abiraterone acetate in the Sample solution (mg/mL)

**Acceptance criteria:** 90.0%–110.0%

**PERFORMANCE TESTS**

**Change to read:**

- **Dissolution** (711)
- **Test 1** (TBD) [NOTE—Protect solutions from light.]

**Buffer:** 56.5 mM of monobasic sodium phosphate in water. Adjust with 5 N sodium hydroxide or phosphoric acid to a pH of 4.5.

**Medium:** 0.25% of sodium lauryl sulfate in Buffer; 900 mL

**Apparatus 2:** 50 rpm

**Time:** 45 min

**Standard solution:** 0.3 mg/mL of USP Abiraterone Acetate RS in Medium prepared as follows. Transfer USP Abiraterone Acetate RS into a suitable volumetric flask. Add 4% of the flask volume of acetonitrile to dissolve, and dilute with Medium to volume.

**Sample solution:** Pass a portion of the solution under test through a suitable filter of 10-μm pore size. Use the filtrate.

**Mobile phase:** Acetonitrile, formic acid, and water (55: 0.05: 45)

**Chromatographic system**
(See Chromatography (621), System Suitability.)

**Mode:** LC
**Detector:** UV 252 nm
**Column:** 4.6-mm × 3-cm; 5-μm packing L1
**Flow rate:** 1 mL/min
**Injection volume:** 10 μL

**System suitability**

**Sample:** Standard solution
**Suitability requirements**

**Tailing factor:** NMT 2.0

**Relative standard deviation:** NMT 2.0%

**Analysis**

**Samples:** Standard solution and Sample solution

Calculate the percentage of the labeled amount of abiraterone acetate \( (C_{26}H_{23}NO_3) \) dissolved:

\[
\left( \frac{r_u}{r_s} \right) \times \left( \frac{C_s}{L} \right) \times V \times 100
\]

- \( r_u \) = peak response from the Sample solution
- \( r_s \) = peak response from the Standard solution
- \( C_s \) = concentration of the Standard solution (mg/mL)
- \( L \) = label claim of abiraterone acetate (mg/Tablet)
- \( V \) = volume of Medium, 900 mL

**Tolerances:** NLT 85% (Q) of the labeled amount of abiraterone acetate \( (C_{26}H_{23}NO_3) \) is dissolved.

**Test 3:** If the product complies with this test, the labeling indicates that it meets USP Dissolution Test 3.

[Note—Protect solutions from light.]

**Buffer:** 56.5 mM of sodium phosphate monobasic in water

**Medium:** 0.25% of sodium lauryl sulfate in Buffer, adjusted with 5 N sodium hydroxide or phosphoric acid to a pH of 4.5; 900 mL

**Apparatus 2:** 50 rpm

**Time:** 45 min

**Standard solution:** 0.3 mg/mL of USP Abiraterone Acetate RS

Acetate RS in Medium prepared as follows. Transfer USP Abiraterone Acetate RS into a suitable volumetric flask. Add 4% of the flask volume of acetonitrile to dissolve, and dilute with Medium to volume.

**Sample solution:** Pass a portion of the solution under test through a suitable filter.

**Mobile phase:** Acetonitrile, formic acid, and water (55:30:15)

**Chromatographic system**

(See Chromatography (621); System Suitability.)

**Mode:** LC

**Detector:** UV 252 nm

**Column:** 4.6-mm × 3-cm; 5-µm packing L1

**Column temperature:** 30° ± 2°C

**Flow rate:** 1.0 mL/min

**Injection volume:** 10 µL

**System suitability**

**Sample:** Standard solution

**Suitability requirements**

**Tailing factor:** NMT 2.0

**Relative standard deviation:** NMT 2.0%

**Analysis**

**Samples:** Standard solution and Sample solution

Calculate the percentage of the labeled amount of abiraterone acetate \( (C_{26}H_{23}NO_3) \) dissolved:

\[
\left( \frac{r_u}{r_s} \right) \times \left( \frac{C_s}{L} \right) \times V \times 100
\]

- \( r_u \) = peak area of each impurity from the Sample solution
- \( r_s \) = peak area of abiraterone acetate from the Standard solution
- \( C_s \) = concentration of USP Abiraterone Acetate RS in the Standard solution (mg/mL)
- \( F \) = relative response factor for each individual impurity (see Table 3)
- \( V \) = volume of Medium, 900 mL

**Acceptance criteria:** See Table 3. Disregard any peak less than 0.05%.

**Tolerances:** NLT 80% (Q) of the labeled amount of abiraterone acetate \( (C_{26}H_{23}NO_3) \) is dissolved. ▲

- **Uniformity of Dosage Units** (905): Meet the requirements

**IMPURITIES**

- **Organic Impurities**

  [Note—Protect solutions from light.]

**Solution A**, Mobile phase, System suitability solution, Standard solution, Sample solution, and Chromatographic system: Proceed as directed in the Assay.

**Sensitivity solution:** 0.3 µg/mL of USP Abiraterone Acetate RS in acetonitrile from Standard solution

**System suitability**

**Samples:** System suitability solution, Standard solution, and Sensitivity solution

**Suitability requirements**

**Resolution:** NLT 1.0 between anhydro abiraterone and 3-deoxy 3-chloroabiraterone peaks, System suitability solution

**Signal-to-noise ratio:** NLT 10, Sensitivity solution

**Relative standard deviation:** NMT 2.0%, Standard solution

**Analysis**

**Samples:** Standard solution and Sample solution

Calculate the percentage of each impurity in the portion of Tablets taken:

\[
\text{Result} = \left( \frac{r_u}{r_s} \right) \times \left( \frac{C_s}{L} \right) \times \left( \frac{1}{F} \right) \times 100
\]

- \( r_u \) = peak response from the Sample solution
- \( r_s \) = peak response from the Standard solution
- \( C_s \) = concentration of USP Abiraterone Acetate RS in the Standard solution (mg/mL)
- \( F \) = relative response factor for each individual impurity (see Table 3)

**Acceptance criteria:** See Table 3. Disregard any peak less than 0.05%.

**Table 3**

<table>
<thead>
<tr>
<th>Name</th>
<th>Relative Retention Time</th>
<th>Relative Response Factor</th>
<th>Acceptance Criteria, NMT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7-Ketoabiraterone acetaete</td>
<td>0.42</td>
<td>1.4</td>
<td>0.50</td>
</tr>
<tr>
<td>a-Epoxyabiraterone acetate</td>
<td>0.62</td>
<td>0.26</td>
<td>0.80</td>
</tr>
<tr>
<td>ß-Epoxyabiraterone acetate</td>
<td>0.66</td>
<td>0.26</td>
<td>0.80</td>
</tr>
<tr>
<td>Abiraterone acetate</td>
<td>1.0</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Abiraterone ethyl ether</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Abiraterone isopropyl ether</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Unspecified impurity</td>
<td>—</td>
<td>1.0</td>
<td>0.20</td>
</tr>
<tr>
<td>Total impurities</td>
<td>—</td>
<td>—</td>
<td>2.0</td>
</tr>
</tbody>
</table>

\( ^a \) This is a process impurity and is controlled in the drug substance monograph. It is included in the table for identification only, and it is not to be reported in the total impurities.

**ADDITIONAL REQUIREMENTS**

- **Packaging and Storage:** Preserve in tight containers, and store at controlled room temperature.

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C228578-M7137-CHM32015, rev. 00 20190927
Add the following:

**LABELING:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if Test 1 is not used.

**USP REFERENCE STANDARDS** (11)

USP Abiraterone Acetate RS
USP Abiraterone System Suitability Mixture RS

It contains Abiraterone Acetate and small amounts of the following:

Abiraterone
17-(Pyridin-3-yl)androsta-5,16-dien-3β-ol.
C\textsubscript{24}H\textsubscript{31}NO \ 349.52

Abiraterone ethyl ether
3β-Ethoxy-17-(pyridin-3-yl)androsta-5,16-diene.
C\textsubscript{26}H\textsubscript{35}NO \ 377.57

Abiraterone isopropyl ether
3β-Isopropoxy-17-(pyridin-3-yl)androsta-5,16-diene.
C\textsubscript{27}H\textsubscript{37}NO \ 391.60

Anhydro abiraterone
17-(Pyridin-3-yl)androsta-3,5,16-triene.
C\textsubscript{24}H\textsubscript{29}N \ 331.50

O-Chlorobutylabiraterone
3β-(4-Chlorobutoxy)-17-(pyridin-3-yl)androsta-5,16-diene.
C\textsubscript{28}H\textsubscript{38}ClNO \ 440.07

3-Deoxy-3-acetyl abiraterone-3-ene
1-[17-(Pyridin-3-yl)androsta-3,5,16-trien-3-yl]ethanone.
C\textsubscript{28}H\textsubscript{30}NO \ 373.53

3-Deoxy 3-chloroabiraterone
3β-Chloro-17-(pyridin-3-yl)androsta-5,16-diene.
C\textsubscript{24}H\textsubscript{30}ClN \ 367.96

α-Epoxyabiraterone acetate
17-(Pyridin-3-yl)-16α,17α-epoxyandrost-5-en-3β-yl acetate.
C\textsubscript{26}H\textsubscript{33}NO\textsubscript{3} \ 407.55

β-Epoxyabiraterone acetate
17-(Pyridin-3-yl)-16β,17β-epoxyandrost-5-en-3β-yl acetate.
C\textsubscript{26}H\textsubscript{33}NO\textsubscript{3} \ 407.55

7-Ketoabiraterone acetate
7-Oxo-17-(pyridin-3-yl)androsta-5,16-dien-3β-yl acetate.
C\textsubscript{26}H\textsubscript{32}NO\textsubscript{3}